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EXAMINER	
CARLSON, KAREN C	
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1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,355	ELLIOTT ET AL.	
	Examiner	Art Unit	
	Karen Cochrane Carlson, Ph.D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *February 26, 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *140-157* is/are pending in the application.

4a) Of the above claim(s) *146-156* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *140-146 and 157* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *Jan/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: front USP 5, 864018 T Alignments

Applicant's election with traverse of Group 11, now claims 140-146, in the reply filed on February 26, 2007 is acknowledged. The traversal is on the ground(s) that it would not be unduly burdensome to examine all inventions relating to SEQ ID NO: 11, its encoding nucleic acid, and antibodies. This is not found persuasive because each is a separate invention requiring separate searches and considerations.

The requirement is still deemed proper and is therefore made FINAL.

Upon search of SEQ ID NO: 11, the encoding nucleic acid was also searched and examined, the protein being the elected invention in the event that In re Ochiae is invoked.

Claims 1-139 have been cancelled. The Examiner has withdrawn Claims 147-156 from further consideration because these claims are drawn to non-elected inventions. Claims 140-146 and 157 are currently under examination.

Benefit of priority is to provisional application 60/410566, filed September 13, 2002, wherein instant SEQ ID NO: 11 is taught as SEQ ID NO: 3 therein.

The substitute specification filed February 14, 2005 has not been entered because it does not conform to 37 CFR 1.125(b) and (c) because: the filing of a substitute specification is to clean up minor errors in the original specification. Instead, throughout the specification there is reference to 42 CADECMs and the supporting tables have been amended to delete information about these CADECMs. Issues of new matter by deletion of all of this information may arise, it is not clear if this national stage application is still considered a 371 of the PCT because it is now effectively a CIP of the PCT, and the oath and declaration may have to be re-submitted. Further, if Applicants intend to file DIVs for

other CADECMs, they would have no basis in this substitute specification and issues of priority would arise.

The substitute specification comprises "interesting" formatting. For example, at page 22, it is not clear what is intended by "=>" in the context of paragraph 2. This is not found in the original specification.

Throughout the specification, there are a lot of "A" and "@" scattered about. See for example page 36, para 4, wherein "AHuman artificial chromosomes@" is set forth. See the entire specification for correction. This is not found in the original specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 140-146 and 157 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claims 140 and 142, the activity of the "biologically active fragment" is not set forth in the claim, rendering the claim indefinite as to what activity is to be assayed to know if a particular fragment meets the claimed limitations.

In Claim 141, it is not clear if it is intended that the polypeptide consisting of a polypeptide comprising SEQ ID NO: 11 is closed or open language. That is, the term "comprising" controls the limitation and the term "consisting of" does not limit the polypeptide to SEQ ID NO: 11.

In Claims 142 and 143, the reference to the fragment to the polypeptide of (a) broadens the scope of the independent claim.

In Claim 144, it is not clear how a nucleic acid that is complementary to an nucleic acid encoding a polypeptide can encode a polypeptide.

In Claim 144 and 157, reference to "at least 90% identical" is not art-recognized. The term "identical" is a qualitative term as in one thing is identical to another or it is not. The term "identity" is the appropriate quantitative term.

In Claim 144 and 157, it is not clear that a polynucleotide that specifically identifies SEQ ID NO: 53 is.

Claim 146 is dependent from Claim 144; it appears that the dependency should be from Claim 145.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 140-146 and 157 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, credible, asserted utility or a well established utility.

The specification is silent regarding the activity of SEQ ID NO: 11. In Table 2 at page 113, SEQ ID NO: 11 is annotated as being related to the receptor for advanced glycation end products (RAGE). However, no where in the specification is there a positive recitation that SEQ ID NO: 11 is expected to have activities associated with RAGE is set forth.

Numerous alternative splice variants of RAGE are known in the art. Those skilled in the art of RAGE splice variants recognize that the splice variants have different functions from RAGE, and even different functions between themselves. The Examiner cites the following references as evidence that splice variants of RAGE are considered to have different structure and function from wild-type RAGE:

Hudson et al. (2006a; Lentivirus gene transfer of the endogenous circulating RAGE splice form blocks mechanisms leading to atherosclerosis. Circulation 114(18 Suppl. S): 25-

26) teach alternatively spliced RAGE resulting from the inclusion of introns 9 (RAGEint9). RAGEint9 reduced S100B stimulated MMP-9 activity and reduced IL-6 when compared to wild-type RAGE. Hudson et al. conclude that RAGEint9 is a novel therapeutic modality to enhance protection against artherosclerotic disease associated with RAGE.

Hudson et al. (2005; A novel method for the detailed analusis of gene splice variants. FASEB J. 19 (4, Supple. S, Part 1): A855) teach numerous splice variants of RAGE and condlude that these variants chang the structure and function of RAGE because they altered the ligand binding domain, extensively removed the extracellular domain, and produced soluble RAGE lacking the transmembrane domain. See also Hudson et al. (2006b; Alternative splicing of the RAGE gene: Analysis and characterization in humans and mice. FASEB J. 20 (5, part 2) A1081).

Schlueter eta l. (2003; Tissue-specific expression patterns of the RAGe receptor and its soluble forms – a result of regulated alternaive splicing? Biochimica et Biophysica Acta 1630: 1-6) teach soluble RAGE lacking the transmembrane and cytoplasmic domains that is an inhibitor of RAGE.

Harashima et al. (2006; Identifiction of mouse orthologue of endogenous secretory receptor for advanced glycation end-products: structure, function and expression. Biochem. J. 396:109-115) teach endogenous secretory RAGE (esRAGE) that is a decoy receptor for RAGE and protects cells and tissues from ligand-dependent injusry such as early retinal complications from diabetes.

Park et al. (2004; Expression of a novel secreted splice variant of the recpetor for advanced glycation end products (RAGE) in human brain astrocytes and peripheral blood mononuclear cells. Molecular Immunology 40: 1203-1211) teach splice variant of RAGE lacking exon 8 and conclude that the diverse expression of RAGE isoforms modify RAGE mediated pathogenesis.

From this survey of the literature, it is evident that SEQ ID NO: 11 is a splice variant of RAGE. The specification does not positively recite a function for SEQ ID NO: 11, and those skilled in the art would not expect this splice variant of SEQ ID NO: 11 to have the same function as RAGE. Therefore, the claimed invention does not have a specific, substantial, credible, asserted utility or a well-established utility.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 140-146 and 157 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 144 and 157 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 144 and 157 refer to a polynucleotide comprising a portion of SEQ ID NO: 53 that "specifically identifies" SEQ ID NO: 53. Upon perusal of the specification, this phrase is not found and Applicants do not address this issue in the claims filed February 14, 2005. Thus, this phrase is new matter.

In Claim 157, no activity is associated with polynucleotides having at least 90% identity to SEQ ID NO: 53 or the fragment of SEQ ID NO: 53. Thus, claim 157 lacks written description. Evidence of possession of these variants include:

Level of skill in the art: The art does not recognize any activity associated with a polypeptide encoded by this fragment or variant.

Complete or partial structure: No activity is associated with the complete or partial structure.

Physical and/or chemical properties: No physical or chemical properties are provided.

Functional characteristics: there are no functional characteristics provided in the specification for the variant or fragment.

Correlation between structure and function: There is no function correlated with structure set forth in the specification.

Method of making the variants: is well-known in the art, but not with respect to assaying the function of the variant.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 140, 142, 144, 145,146 and 157 are rejected under 35 U.S.C. 102(b) as being antipated by Morser et al. (USP 5,864,018). The sequence alligments are attached to the front page of Morser et al. and are being mailed to Applicants.

Morser et al. teach RAGE as Morser et al. SEQ ID NO: 2, wherein amino acids 1-274 are identical to amino acids 1-274 of instant SEQ ID NO: 11. The soluble form of RAGE is

Morser et al's SEQ ID NO: 4 which lacks the N-terminal 22 amino acids. Therefore, Morser et al. teach a polypeptide comprising a biologically active fragment of SEQ ID NO: 11 (**Claim 140b; 142**) or an immunogenic fragment of SEQ ID NO: 11 (**Claim 140c; 143**).

While whether the polypeptide is made recombinantly or not does not effect the polypeptide. However, in Example 1 at Col. 20, Morser et al. teach the recombinant production of the soluble RAGE (**Claims 145, 146**).

Morser et al. teach nucleic acid encoding RAGE as Morser et al.'s SEQ ID NO: 1, and soluble RAGE as SEQ ID NO: 3. Therefore, Morser et al. teach a polypeptide encoded by a polynucleotide that identifies SEQ ID NO: 53 (**Claim 144c**) that is linked to a promoter sequence (Example 1; **Claim 144f**). Morser et al. teach a polynucleotide that identifies SEQ ID NO: 53 (**Claim 157c**).

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 571-272-0946. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen Cochrane Carlson PhD

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KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER